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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.          | CONFIRMATION NO.       |
|---|-------------|----------------------|------------------------------|------------------------|
| 10/539,049  | 03/31/2006  | Frank Slade Abbott   | U0080645/TWB                 | 7391                   |
| 720 7590 02/01/2008<br>OYEN, WIGGS, GREEN & MUTALA LLP<br>480 - THE STATION<br>601 WEST CORDOVA STREET<br>VANCOUVER, BC V6B 1G1<br>CANADA |             |                      | EXAMINER<br>LAO, MARIALOUISA |                        |
|   |             |                      | ART UNIT<br>1621             | PAPER NUMBER           |
|   |             |                      | MAIL DATE<br>02/01/2008      | DELIVERY MODE<br>PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                               |                               |  |
|------------------------------|-------------------------------|-------------------------------|--|
| <b>Office Action Summary</b> | Application No.<br>10/539,049 | Applicant(s)<br>ABBOTT ET AL. |  |
|                              | Examiner<br>M. Louisa Lao     | Art Unit<br>1621              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) 4-8, 10-27 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9 and 28-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. <u>1/2/08</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>09/21/05</u> . | 6) <input type="checkbox"/> Other: _____   |

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of claims 1, 2, 3, 9 and 28-40 in the reply filed on 10/23/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Applicants elected the species of compounds 20 and 21 (i.e. 2(E)-4,4,-difluoro-2-2-propypent-2-enoic acid and 2(Z)-4,4,-difluoro-2-2-propypent-2-enoic acid) claim 27 on page 7 on 12/18/07.
3. Claims 4-8, 11-27 and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/23/07.
4. The requirement is still deemed proper and is therefore made FINAL.
5. For purposes of examination, the species elected including the first method of use (for seizures) and the first method of synthesis of the elected species (compounds on page 37 of the instant specification, scheme 6 on page 35) are evaluated on the merits.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 35-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound of Formula I, as recited, does not reasonably provide

enablement for prodrugs thereof and the method of treating a patient comprising administering a prodrug thereof. The specification does not enable the person skilled in the art of synthetic chemistry, to make the invention commensurate in scope with these claims. The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art, and, h) the breadth of the claims.

8. In the present case, the important factors leading to a conclusion of undue experimentation are the absence of any working example of formed prodrugs, the lack of predictability in the art, and the broad scope of the claim.

*c) the presence or absence of working examples.* There are no working examples of prodrugs of formula I that are formed. Claim 35 is drawn to “a prodrug transformable *in vivo* to a compound according to claim 1”, yet the various examples presented are found deficient to produce “... prodrugs thereof”.

*g) the predictability or unpredictability of the art.* The states of the art of making prodrugs are unpredictable, since this art is empirical in nature.

*For prodrugs,* the state of the art is unpredictable and at best, an empirical science which requires fulfilling a rationale for the optimization of absorption, distribution, metabolism, and excretion of a drug. Determining whether a compound meets the attributes of a useful prodrug entails substantial clinical testing with laborious experimentation. See Wikipedia website on the subject.

*h) the breadth of the claim.* Claim 35 is broad since encompasses the plurality inclusive of *all* the "... *prodrugs thereof*" of formula I.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.Cir.1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1, 2, 3, 9 and 28-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The elected species of 2(E)-4,4,-difluoro-2-2-propyent-2-enoic acid and 2(Z)-4,4,-difluoro-2-2-propyent-2-enoic acid) in claim 27 on page 7 recite compounds that are not recited in the limitations of "formula (I)" and the substituents thereto. There is insufficient antecedent basis for these elected species.

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 2, 3, 9 and 28-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohuchida et al. (US7176240, US'240) and Palaty et al. *J. Med. Chem.* 1995, 38, 3398-3406. in view of Bennani (US6521790, US'790).

15. The instant claims are drawn to a compound selected from the group consisting of compounds represented by the formula (I) and stereoisomers and pharmaceutically acceptable salts, with substituents as therein recited; a method of treating seizures, a pharmaceutical composition, a method of synthesizing of the elected species using scheme 6.

16. US'240 (see abstract) teaches compounds of formula (I), wherein R<sup>1</sup> is alkyl substituted by fluorine(s) and R<sup>2</sup> is hydroxy and teaches the Applicants' Scheme 6 reaction steps in columns 23 and 27; while Palaty et al. (see column 2 page 3398 compounds 1 and 7) teaches compounds of formula (I), wherein R<sup>2</sup> is hydroxy.

17. The instant claims differ from US'240 in that US'240 lacks the double bond; but Palaty et al.'s compounds 1 and 7 show single and double bonds, which exhibit use for anti-convulsive activities.

18. The instant claims differ from US'240 and Palaty et al. in the specificity of utility. US'240 shows the utility of for the treatment of neuronal dysfunction, Palaty et al. is used for anti-convulsive activities.

19. However, US'790 is relied upon to show in columns 1-3 that the compounds akin to compounds of both US'240 and Palaty et al. are useful for both anti-convulsive activities and seizures, including *inter alia* bipolar disorders, pain due to migraine.

20. At the time of Applicants' invention, one of ordinary skill in the art looking for fluorinated valproate analogues, would have found it *prima facie* obvious to start with the teachings of US'240 and Palaty et al. since both cited art references are geared towards valproate analogues.

21. An artisan would have been motivated to employ the teachings of US'240 and Palaty et al. since US'240 and Palaty et al. teach the analogs of single and double bonds and the substituents of fluorine atom(s) that can be on the alkyl group (i.e. fluoroalkyl); with a reasonable expectation that other fluorinated and/or unsaturated valproate analogues can be successfully made.

22. No claims are allowed.

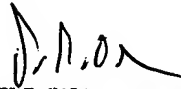
### *Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair->

Application/Control Number:  
10/539,049  
Art Unit: 1621

Page 7

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PETER O'SULLIVAN  
PRIMARY EXAMINER  
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MLouisa Lao  
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